

REMARKS

The specification has been amended to insert the serial number of co-pending U.S. Application No. 10/622,293.

Claims 1-65 were pending in this application. Claims 8-11 and 26-49 have been withdrawn by the Examiner as being drawn to non-elected inventions.

Applicant has canceled claims 1-49 and 64, without prejudice, and fully reserves the right to prosecute the subject matter of the canceled claims in one or more related applications.

Applicant has also amended claims 50, 56, 60, and 65 and added new claims 66-69 to clarify the presently claimed invention. Specifically, claim 50 has been amended to recite that the biocompatible material is in the form of a scaffold. Support for the amendment can be found in the specification at, *inter alia*, page 1, lines 11-12; page 6, lines 1-3; and canceled claim 64.

New claims 66 and 67 have been added to recite a method for treating a defective, diseased, damaged or ischemic tissue or organ in a subject comprising implanting (claim 66) or injecting (claim 67) the biocompatible material of claim 50 into the subject. New claims 68 and 69 have been added to recited a method for augmenting or reconstructing a tissue or organ in a subject comprising implanting (claim 68) or injecting (claim 69) the biocompatible material of claim 50 into the subject. Support for the new claims can be found in the specification at, *inter alia*, page 5, lines 10-23; and page 14, line 32, to page 15, line 10.

The dependency of claims 56, 60, and 65 has been amended. No new matter has been added.

Upon entry of the amendments, claims 50-63 and 65-69 will be pending in this application.

I. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

1. The Pending Claims Are Not Anticipated by Abatangelo

Claims 1-6, 12-22, 24-25, 50-60, and 64-65 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Abatangelo *et al.* (WO 97/18842, "Abatangelo"). Specifically, the Examiner alleges that Abatangelo teaches a biological material comprising extracellular bone marrow free of cellular components (or decellularized) and its use in tissue grafts (or are combined with biological materials).

As a preliminary matter, claims 1-6, 12-22, and 24-25 have been canceled and thereby rendering the rejection moot with respect to these claims. For the following reasons, Applicant respectfully submits that Abatangelo does not teach or suggest amended claim 50 and its dependent claims.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. *W.L. Gore Associates v. Garlock, Inc.*, 721 F.2d 1540, 1554, 220 U.S.P.Q. 303, 314 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); *In re Donohue*, 766 F.2d 531, 226 U.S.P.Q. 619 (Fed. Cir. 1985). To anticipate a patent claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. *MEHL/Biophile International Corp. v. Milgraum*, 192 F.3d 1362, 52 U.S.P.Q.2d 1303 (Fed. Cir. 1999); *In re Robertson*, 169 F.3d 743, 49 U.S.P.Q.2d 1949 (Fed. Cir. 1999).

Abatangelo's decellularized extracellular matrix is structurally different from the decellularized extracellular matrix of the present invention which is obtained from bone marrow extracellular matrix which has been produced *in vivo* in an animal.¹ Abatangelo discloses decellularized extracellular matrix obtained from extracellular matrix (a) secreted by either (i) an efficient culture of autologous or homologous bone marrow stem cells partially or completely differentiated into specific connective tissue cells, or (ii) specific homologous mature connective tissue cells, and (b) grown on a three-dimensional biocompatible and biodegradable matrix consisting of a hyaluronic acid derivative (see Abatangelo, Abstract; and page 3, line 19, to page 4, line 6). Contrary to the Examiner's allegation, Abatangelo does not teach or suggest decellularized bone marrow extracellular matrix obtained from bone marrow extracellular matrix produced *in vivo* in an animal, as recited in amended claim 50. Instead, the decellularized bone marrow extracellular matrix of Abatangelo is obtained from extracellular matrix produced by (i) connective tissue cells

¹ Applicant respectfully submits that "bone marrow extracellular matrix...produced *in vivo* in an animal" is not a process limitation, and even if it were, such limitation imparts the presently claimed biocompatible material with distinctive structural characteristics. As stated in the MPEP, "[t]he structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where...the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product." MPEP § 2113 citing *In re Garnero*, 412 F.2d 276, 279.

coming from partially or completely differentiated bone marrow stem cells (see Abatangelo, page 4, lines 10-12), or (ii) mature connective tissue cells (see Abatangelo, page 5, lines 2-3) in culture (*i.e.*, not *in vivo*). Since the starting materials used to produce the extracellular matrix used in the present invention (*i.e.*, bone marrow obtained *in vivo*) and Abatangelo (*i.e.*, connective tissues grown and developed *in vitro*) are different, the decellularized extracellular matrix of the present invention is different from the decellularized extracellular matrix of Abatangelo.

For the foregoing reasons, Abatangelo does not teach or suggest the decellularized bone marrow extracellular matrix of amended claim 50. Thus, amended claim 50, and its dependent claims, are not anticipated by Abatangelo. Applicant respectfully submits that the rejection is in error and should be withdrawn.

2. The Pending Claims Are Not Anticipated by Lee or Peters

Claims 1-5, 12-21, 24-25, 50-59, and 62-63 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Lee *et al.* (Biochim Biophys Acta. 1999 Aug 5;1428(2-3):300-4, "Lee") or Peters *et al.* (Am J Med Sci. 1995 May;309(5):285-94, "Peters"). Specifically, the Examiner alleges that Lee teaches a composition comprising decellularized bone marrow from fetal bovines, and Peters teaches a composition comprising decellularized bone marrow.

As a preliminary matter, claims 1-5, 12-21, and 24-25 have been canceled and thereby rendering the rejection moot with respect to these claims. Although Applicant does not agree and in no way acquiesces with the rejection, solely to expedite prosecution and obtain coverage for certain embodiments of the present invention, claim 50 has been amended to recite the subject matter of claim 64, which was not rejected by the Examiner as being anticipated by Lee or Peters. In particular, amended claim 50 recites a biocompatible material in the form of a scaffold. Applicant respectfully submits that the rejection is obviated and should be withdrawn.

II. THE CLAIM REJECTIONS UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN

Claims 1-7, 12-25, and 50-65 are rejected under 35 U.S.C. § 103(a) ("Section 103") as allegedly being unpatentable over Abatangelo in view of Cobb *et al.* (U.S. Patent 6,241,981, "Cobb"). Specifically, the Examiner alleges that while Abatangelo does not teach the composition further comprising vascular endothelial growth factor (VEGF), Cobb teaches

that at the time of the claimed invention, VEGF was known and used in the art with tissue grafts.

As a preliminary matter, claims 1-7 and 12-25 have been canceled and thereby rendering the rejection moot with respect to these claims. For the following reasons, Applicant respectfully submits that amended claim 50, and its dependent claims, are patentable over Abatangelo in view of Cobb.

To reject claims in an application under 35 U.S.C. § 103(a), the Patent Office bears the initial burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 U.S.P.Q.2d 1529, 1530 (Fed. Cir. 1993). To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references, either alone or in combination, must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

Applicant respectfully submits that a *prima facie* case of obviousness has not been made with regard to amended claim 50 and its dependent claims. First, there is no suggestion or motivation in either Abatangelo or Cobb to modify or combine the reference teachings. Abatangelo and Cobb relate to different technical problems. On one hand, Abatangelo teaches tissue graft constructs useful to address the current inefficiencies in skin/dermal substitutes (see Abatangelo, page 1, line 9, to page 3, line 17). On the other hand, Cobb relates to tissue graft constructs useful in promoting regrowth and healing of damaged or diseased neurological related tissue structures (see Cobb, Abstract). Applicant submits that one skilled in the art of neurological tissue repair would find no suggestion or motivation to apply the teaching of Abatangelo, which relates to skin tissue repair. Likewise, one skilled in the art of skin tissue repair would find no suggestion or motivation to apply the teaching of Cobb, which relates to neurological tissue repair. In fact, Cobb never mentions as a source of extracellular matrix the use of bone marrow, which is essential to the methods of Abatangelo.

Even assuming *arguendo* that the teaching of Abatangelo and Cobb can be modified or combined, which they cannot, Applicant submits that there is no reasonable expectation of

success offered by Abatangelo in view of Cobb to arrive at the claimed biocompatible material. As discussed above, Abatangelo relates to skin tissue repair and Cobb relates to neurological tissue repair. Since skin tissue repair and neurological tissue repair are significantly different conditions, the skilled artisan would not expect that the treatment for one condition could successfully be used to treat the other condition. Therefore, based on these cited references, one skilled in the art would have no reasonable expectation of arriving at the claimed invention.

Finally, Abatangelo and Cobb, either alone or together, do not teach or suggest each and every claim limitation. As discussed above, Abatangelo discloses decellularized bone marrow extracellular matrix obtained from bone marrow extracellular matrix produced in culture, and not from bone marrow extracellular matrix produced *in vivo* in an animal, as recited in amended claim 50. Cobb never mentions bone marrow, much less teach or suggest decellularized bone marrow extracellular matrix obtained from bone marrow extracellular matrix produced *in vivo*, as recited in amended claim 50. Accordingly, Cobb does not cure the deficiency of Abatangelo and therefore, the references, even in combination, do not teach or suggest all claim limitations.

Finally, the Examiner has improperly used hindsight reconstruction to pick and choose among isolated disclosures in Abatangelo and Cobb to reconstruct the claimed invention. In particular, Applicant respectfully submits that *hindsight reconstruction* has been used in the rejection of the present invention to combine skin tissue repair and neurological tissue repair. Such hindsight, however, is improper and should be avoided in determining patentability. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1 U.S.P.Q.2d 1593 (Fed. Cir. 1987), *cert. denied*, 481 U.S. 1052 (1987).

In view of the foregoing, Applicant respectfully submits that a *prima facie* case of obviousness is not established, and requests the Examiner to withdraw the Section 103 rejection.

CONCLUSION

Applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application. Withdrawal of the Examiner's rejections and an allowance of the application are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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Enclosures